SLC22A12 gene

solute carrier family 22 member 12

Normal Function

The *SLC22A12* gene provides instructions for making a protein called urate transporter 1 (URAT1). This protein is found in the kidneys, specifically in structures called proximal tubules. These structures help to reabsorb needed nutrients, water, and other materials into the blood and excrete unneeded substances into the urine. Within the proximal tubules, the URAT1 protein helps transport molecules by exchanging negatively charged atoms (anions) for a substance called uric acid. Uric acid is a byproduct of certain normal chemical reactions in the body. In the bloodstream it acts as an antioxidant, protecting cells from the damaging effects of unstable molecules called free radicals. However, having too much uric acid in the body is toxic, so excess uric acid is removed from the body in urine. The URAT1 protein helps reabsorb uric acid (or a similar version of this substance called urate) into the bloodstream or release it into the urine, depending on the body's needs. Most uric acid that is filtered through the kidneys is reabsorbed into the bloodstream; about 10 percent is released into urine.

Health Conditions Related to Genetic Changes

renal hypouricemia

More than 30 mutations in the *SLC22A12* gene have been found to cause renal hypouricemia. This condition results in a reduced amount of uric acid in the blood. Renal hypouricemia often does not cause any health problems but can lead to pain and nausea after exercise, kidney stones, or blood in the urine (hematuria). Most of the mutations that cause renal hypouricemia replace single protein building blocks (amino acids) in the URAT1 protein and reduce the protein's ability to reabsorb uric acid into the bloodstream. The most common mutation in affected Japanese and South Korean individuals replaces the amino acid tryptophan at position 258 with a premature stop signal (Trp258Ter or W258X), resulting in an abnormally short protein. A reduction in URAT1's ability to reabsorb uric acid results in a shortage of uric acid in the blood and an excessive amount lost through the urine. While it is not clear how these changes in uric acid levels lead to the signs and symptoms of renal hypouricemia, it is likely that the loss of uric acid's antioxidant properties in combination with the increase in uric acid passing through the kidneys to be released in urine contribute to the characteristic features of this condition.

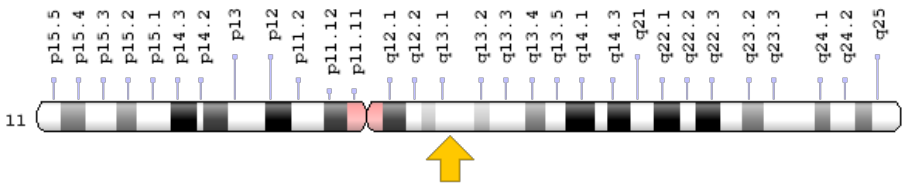
other disorders

Some studies have found variations in the *SLC22A12* gene to be associated with a condition called gout, which is a form of arthritis resulting from uric acid crystals in the joints. These variants likely impair the URAT1 protein's ability to release uric acid into the urine. As a result, too much uric acid is reabsorbed into the bloodstream, causing a buildup of uric acid in the body. This excess uric acid often accumulates in the body's joints in the form of crystals, leading to painful arthritis. Other studies, however, have not found an association between *SLC22A12* gene variants and gout. While the role of the *SLC22A12* gene in gout may be unclear, it is known that a combination of lifestyle, genetic, and environmental factors play a part in determining the risk of this complex disorder.

Chromosomal Location

Cytogenetic Location: 11q13.1, which is the long (q) arm of chromosome 11 at position 13.1

Molecular Location: base pairs 64,590,810 to 64,603,250 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- OAT4L
- organic anion transporter 4-like protein
- renal-specific transporter
- RST
- solute carrier family 22 (organic anion/cation transporter), member 12
- solute carrier family 22 (organic anion/urate transporter), member 12
- URAT1
- urate anion exchanger 1
- urate transporter 1

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Purines Are Degraded to Urate in Human Beings
  https://www.ncbi.nlm.nih.gov/books/NBK22372/#A3526

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SLC22A12%5BTIAB%5D%29+OR+%28URAT1%5BTIAB%5D%29+OR+%28urate+transporter+1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- SOLUTE CARRIER FAMILY 22 (URATE TRANSPORTER), MEMBER 12
  http://omim.org/entry/607096

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SLC22A12%5Bgene%5D
- HGNC Gene Family: Solute carriers
  http://www.genenames.org/cgi-bin/genefamilies/set/752
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=17989
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/116085
- UniProt
  http://www.uniprot.org/uniprot/Q96S37

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